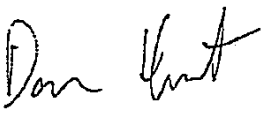
Test Material:	Flufenacet
MRID	46997402
Title:	Flufenacet (FOE 5043) – Small Scale Prospective Ground-Water Monitoring Study, Minden, Nebraska, 1995.
EPA PC Code:	121903
OCSPP Guideline:	835.7100

For Cambridge Environmental

Primary Reviewer: Dan Hunt **Signature:** 

Date: 7/03/12

Secondary Reviewer: Joan Harlin **Signature:** 

Date:

QC/QA Manager: Joan Gaidos **Signature:** 

Date:

Small-Scale Prospective Ground-Water Monitoring Study of Flufenacet

The ground water monitoring of flufenacet was studied in a 3-acre corn plot (silt loam soil) in Nebraska.

Report: MRID 46997402. Dyer, D.G. and K.K. Helfrich. 2005. Flufenacet (FOE 5043) – Small Scale Prospective Ground-Water Monitoring Study, Minden, Nebraska, 1995. Unpublished study performed by Bayer CropScience, Stilwell, KS (analytical phase); LFR Levine Fricke, Tallahassee, FL (field phase); and Alta Analytical Laboratory Inc., El Dorado Hills, CA (analytical phase; p. 15); sponsored and submitted by Bayer CropScience, Research Triangle Park, NC. Project ID Nos.: Bayer CropScience: F3212402; LFR Levine Fricke: 004-03548-00; Alta Analytical Laboratory: 1397. Experiment initiation June 11, 1995 (application) and completion October 6, 2004 (analysis completed; p. 15). Final report issued August 8, 2005.

Document No.: MRID 46997402

Guideline: OCSPP 835.7100

Statements: The study was conducted in accordance with the USEPA FIFRA Good Laboratory Practice (GLP) standards (40 CFR Part 160), with noted exceptions (p. 3). Signed and dated Data Confidentiality, GLP, Quality Assurance, and Certification of Authenticity statements were provided (pp. 2-5).

Classification: This study is **Acceptable**. The test site did not receive adequate water input during the initial month of the study; the stability of flufenacet and its transformation products in ground water samples was not properly demonstrated; and a five-year plot use history was not provided. No significant deviations from good scientific practices were noted.

PC Code: 121903

Reviewer: Gabriel Rothman
Environmental Scientist, USEPA

Signature: Gabe Rothman
Date: 9/24/15

EXECUTIVE SUMMARY

Flufenacet (*N*-(4-fluorophenyl)-*N*-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]acetamide; applied as Axiom DF, 54.8% a.i.) was applied to a bare plot (3.0 acres) at a target rate of 1.01 kg flufenacet/ha (0.9 lb flufenacet/A) on June 11, 1995 near Minden, Nebraska. The target application rate was 110% of the maximum label rate. The test application was made to bare soil, four days following planting with corn. Potassium bromide (KBr) was used as a tracer and applied following the test substance application at a target application rate of 50 lb KBr/A. The experiment was carried out in accordance with the USEPA Pesticide Assessment Guidelines Subdivision N, 166-1, and in compliance with the USEPA FIFRA (40 CFR, Part 160) GLP standard, with minor exceptions. The test site was located in a setting described as "less vulnerable" to ground water contamination. The soil was characterized as silt loam in the top 19 ft, overlaying loam (19-23 ft), and sandy loam (>23 ft).

The application rate was verified using Petri dishes (3.5-inch diameter) and aluminum trays (14.875 x 10.25 inch) containing a thin layer of sieved (2 mm) control soil that was placed in the test plot prior to the test application. Mean recovery of flufenacet from the Petri dishes was 114% of the label rate, and mean recovery of flufenacet from the aluminum trays was 112% of the label rate.

Soil samples were collected from the treated plot prior to the test application and at 0, 1, 3, 8, 15, 29, 57, 93, 181, 286, 374, 486, and 557 days posttreatment to a depth of 1 ft. Samples were composited to form three composite samples per sampling interval.

Soil-pore water and ground water was collected prior to test treatment and at 9 (soil-pore water only), 16, and 30 days, then *ca*. monthly through 741 days posttreatment, then quarterly through 1740 days posttreatment for soil-pore water samples or 3102 days for ground water samples to monitor analyte behavior in the unsaturated and saturated zones. Soil-pore water and ground water were collected from six instrumentation clusters installed in the treated plot, with each cluster containing one deep monitoring well, one shallow monitoring well, and two suction lysimeters installed at depths of approximately 3, 6, 9, and 14 feet below ground surface (bgs). Shallow wells were installed so that their screened intervals (10 ft in length) intersected the top 2-3 feet of ground water surface, and deep wells were installed so that their screened intervals (*ca*. 5 ft in length) were positioned immediately below the shallow well screened interval.

Soil, lysimeter water, and ground water were analyzed for flufenacet and the transformation products flufenacet alcohol, flufenacet oxalate, flufenacet sulfonic acid, and flufenacet thiadone, with separate samples analyzed for Br. Soil samples were extracted by shaking for one hour with acetonitrile:0.1N HCl (1:1, v:v) and centrifuged, and the extracts were combined with methanol, evaporated and then adjusted to 5 mL with 0.1% formic acid and filtered (0.45 µm) prior to analysis by LC/MS/MS. Water samples were acidified with 1N HCl, passed through a octadecyl (C18) SPE column, and the analytes were eluted with methanol, concentrated to *ca*. 1 mL, brought to volume with 0.1% formic acid, and syringe filtered (0.45 µm) prior to analysis by LC/MS/MS. The LOQ was 10 µg/kg for each analyte in soil, and the LOQ was 0.1 µg/L for each analyte in water.

The site did not receive any rainfall or irrigation until 12 days after the test application (0.32 inches; June 23, 1995), followed by *ca*. 1.3 inches at 17-19 days posttreatment (June 28-30, 1995). Total water input during the first growing season (June 11-October 31) was 24.76 inches or 128% of the

150% moisture input target. For subsequent years, total water input during the growing season (May 1-October 31) was 20.60, 24.58, 22.87, 34.12, 18.35, 30.70, 45.70, and 20.24 inches, respectively, which equaled 115%, 137%, 128%, 190%, 102%, 171%, 255%, and 113% of the 30-yr average precipitation of 17.93 inches. Total cumulative water input through December 8, 2003 (102 months posttreatment) was 289.62 inches or 139% of the prorated average rainfall of 208.35 inches (excluding 17.70 inches of water received as snowfall (177 inches) during the study period).

Data indicate that flufenacet dissipated quickly in soil and was not detected in soil-pore water (1 of 610 samples) or ground water samples (1 of 482 samples) analyzed through 1645 days and 3102 days, respectively. Flufenacet sulfonic acid was the primary transformation product detected in soil-pore water and ground water samples, with lower amounts of flufenacet oxalate and flufenacet thiadone also detected. Residues of the transformation products peaked and declined in all ground water wells detected during the course of the study period.

The **bromide tracer** was first observed in the 3-, 6-, and 9-ft lysimeters at 30 days posttreatment and in the 14-ft lysimeter at 94 days posttreatment, with Br levels reaching average maximum concentrations at 119 days in the 3-ft lysimeter, at 468 days in the 6-ft lysimeter, at 665 days in the 9-ft lysimeter, and at 897 days in the 14-ft lysimeter. The Br tracer first appeared in the shallow ground water at elevated levels at 119 days (in the southeast cluster only) and appeared in the other five shallow wells from 994-1565 days posttreatment, followed by the deep monitoring wells by 375 days (southeast cluster) or 1155-2021 days (all other clusters).

The mean measured concentration of flufenacet in the 0-15 cm soil depth was a maximum of 523 ppb at 1 day, which is *ca*. 80% of the theoretical (reviewer-calculated) and decreased to 320 ppb by 15 days, 220 ppb by 29 days, 44 ppb by 57 days, and declined to <LOQ by 468 days posttreatment. Flufenacet had a DT_{50} value of 21.1 days in soil, calculated from the 0-15 cm soil residue data following the maximum detection at 1 day posttreatment (single first order model). The transformation products flufenacet alcohol, flufenacet oxalate, flufenacet sulfonic acid, and flufenacet thiadone were all detected at low levels (<LOQ) in the top 0-15 cm soil depth, with only flufenacet oxalate and flufenacet sulfonic acid detected at a mean concentration above the LOQ (both detected at 10 ppb at 29 days). Transformation products were not detected in soil following 286 days posttreatment.

Flufenacet was detected in only 1 of 610 soil-pore water samples, at a level below the LOQ at 30 days (6-ft depth). Flufenacet sulfonic acid was the most prevalent transformation product detected in soil-pore water samples, detected in 104 of 610 samples. Flufenacet sulfonic acid was first detected in soil-pore water at 58 days (3-, 6-, and 9-ft depths; *ca*. 1 month following detection of the Br tracer), was a maximum of 5.20 ppb in the 3-ft depth (at 119 days), 3.80 ppb in the 6-ft depth (at 412 days), 1.00 ppb in the 9-ft depth (at 94 days) and 1.40 ppb in the 14-ft depth (at 897 days). Flufenacet oxalate was detected in 22 of 610 samples, and at a maximum of 0.33 ppb in the 9-ft depth at 94 days. Residues declined to background by 665 days and 1254 days for flufenacet oxalate and flufenacet sulfonic acid, respectively. Flufenacet alcohol and flufenacet thiadone were generally not detected in soil-pore water, with only 2-5 detections each, below the LOQ, in 610 samples.

Flufenacet was not detected in shallow or deep ground water samples, excluding one detection below the LOQ prior to breakthrough of the tracer. Flufenacet sulfonic acid was the most prevalent transformation product detected in ground water samples, detected in 107 of 482 samples, with

residues detected above the LOQ in only 3 of the 6 well clusters. Flufenacet sulfonic acid was first detected in the shallow ground water in the southeast cluster at the LOQ at 93 days, one sampling interval prior to detection of the tracer, and did not appear in another cluster at a level above the LOQ until 1061 days. Flufenacet sulfonic acid residues peaked in the shallow ground water of the southeast cluster at 0.66 ppb at 501-534 days, then declined to <LOQ by 895 days, with residues peaking in other shallow wells at 1155 days and 2210 days. Flufenacet sulfonic acid was first detected above the LOQ in the deep wells at 412 days in the southeast cluster, *ca*. 1 month after breakthrough of the tracer, increased to a maximum of 0.27-0.28 ppb by 534-664 days, then declined to <LOQ by 994 days posttreatment. Flufenacet sulfonic acid first appeared in two other clusters, above background levels, at 805 days and 1565 days, respectively, with maximums of 0.23 ppb in the south central cluster at 1412 days and 0.27 ppb in the northeast cluster at 2299 days. Flufenacet thiadone was detected in 39 of 482 ground water samples, with residues generally limited to the southeast and south central clusters; maximum flufenacet thiadone residues were 0.18 ppb for shallow wells (at 501 days) and near the LOQ for deep wells (at 664 days). Flufenacet oxalate was not detected above the LOQ in shallow and deep ground water samples, excluding one detection near the LOQ (0.12 ppb in the shallow well at 149 days), and flufenacet alcohol was only detected in one ground water sample, at a level below the LOQ. Flufenacet and its transformation products were not detected in ground water samples from the control plot, excluding a few sporadic detections near the MDL.

MATERIALS AND METHODS

Test site: The test site was located four miles northwest of Minden, Nebraska, in Kearney County (40°33’02” N; 99°02’15” W) on the eastern edge of an active 40-acre cornfield (pp. 17-18; Figure 1, p. 303; Appendix 2, p. 232; Table 1, p. 264). The site was described as “less vulnerable” to ground water contamination (p. 14). The test site consisted of a 3.0-acre test plot (average slope <1%) and a 1.0-acre control plot located hydraulically up-gradient from the test plot (Appendix 2, Figure 2, p. 304). The soil at the test site was characterized as silt loam (predominantly Coly-Kenesaw soil series) in the top 19 ft, overlaying loam (19-23 ft) and sandy loam (>23 ft; Table 1, p. 44; Appendix 2, p. 233; Figure 4, p. 306). The nearest surface water body was not reported. Soil hydraulic conductivity in the unsaturated zone, determined by constant-head permeameter tests in six boreholes in the field on May 30, 1996, was a mean of 0.820 cm/hr at the 1-ft depth and 0.681 cm/hr at the 3-ft depth (overall mean of 0.751 cm/hr; pp. 18, 28; Appendix 2, p. 235). Additional hydraulic conductivity measurements of undisturbed soil cores were determined in the laboratory from four Shelby tube cores that were analyzed at various depths from 0-22 feet bgs and gave variable results ranging from 0.00 to 7.16 cm/hr (pp. 18, 28; Appendix 2, pp. 235-236). The mean saturated zone hydraulic conductivity at the site, measured on April 23, 1996, was 1.8 ft/day (range from 0.55 to 2.58 ft/day), determined from rising head slug tests performed in three monitoring wells installed within the test site (pp. 18, 29; Appendix 2, Table 13, p. 281). The depth to ground water, measured from six monitoring wells within the test plot and four observation wells (piezometers) installed outside the four corners of the test plot for 102 months beginning in May 1995, ranged from 20.6 to 33.3 ft below ground surface (bgs) and showed a seasonal variation, with the deepest levels observed in the final months of the study (pp. 18-19, 29; Appendix 2, Table 14, pp. 282-293; Figure 16, p. 321). The direction of ground water flow was estimated to be to the northeast, with ground water flow velocities ranging from 0.003-0.027 ft/day (mean of 0.0136 ft/day; p. 29; Appendix 2, pp. 254-255). The soil profile was homogenous across the study site, with

no indication of any restrictive soil horizons; however, a test pit was not excavated (Appendix 2, Figures 6-7, pp. 308-309). A plot history was not reported.

Soils: On March 24-25, 1995, **s**amples were collected from four borings in 15-cm increments to a depth of 5 ft, and then at 2-ft intervals to *ca*. 25 feet below ground surface (bgs) for soil characterization (p. 18; Table 1, p. 44; Appendix 2, pp. 233-234).

Properties of the soil from the test site, 0-5 ft.

Property	Depth (ft)									
	0.0-0.5	**0.5-1.0**	**1.0-1.5**	**1.5-2.0**	**2.0-2.5**	**2.5-3.0**	**3.0-3.5**	**3.5-4.0**	**4.0-4.5**	**4.5-5.0**
Textural classification	SiL	SiL	SiL	SiL	SiL	SiL	SiL	SiL	SiL	SiL
% sand	27.3	25.7	24.3	23.0	25.0	24.0	24.7	24.3	24.0	23.0
% silt	54.3	57.3	59.7	61.3	60.3	62.3	63.3	63.7	64.0	64.3
% clay	18.3	17.0	16.0	15.7	14.7	13.7	12.0	12.0	12.0	12.7
pH	7.6	7.6	7.7	7.7	8.0	8.2	8.3	8.4	8.4	8.4
Organic matter (%)	1.17[2]	0.92	0.72	0.77	0.53	0.25	0.28	0.68	0.27	0.28
CEC (meq/100 g)	22.2[2]	23.1	23.0	21.7	21.2	22.3	23.7	24.8	23.0	19.1
Bulk density (g/cm^3)	1.02[2]	1.04	1.04	1.05	1.04	1.05	1.05	1.03	1.04	1.04
Moisture at 1/3 atm (%)	27.4	28.0	26.6	27.7	27.3	28.0	26.6	27.1	27.7	27.2
Taxonomic classification (e.g., ferro-humic podzol)[1]	Coly soil series: Fine-silty, mixed, superactive, calcareous, mesic Typic Ustorthent Kenesaw soil series: Coarse-silty, mixed, superactive, mesic Typic Haplustoll									
Soil mapping unit										

Data were obtained from Table 1, p. 44 of the study report. Taxonomic and textural classifications were obtained/confirmed from the reviewer from the NRCS website. SiL = Silt loam.

1 It was reported that the Coly soil series comprised *ca*. 60-65% of the map area vs. *ca*. 30-35% for the Kenesaw soil series, and that lesser areas of Hobbs silt loam were also present (Appendix 2, p. 233; Figure 4, p. 306 of the study report).

2 Averages differed slightly from values reported in Appendix 2, Table 2, p. 265 of the study report.

Properties of the soil from the test site, 5-25 ft.

Property	Depth (ft)					
	5.0-7.0	**7.0-9.0**	**9.0-15.0**	**15.0-19.0**	**19.0-23.0**	**>23**
Textural classification	Silt loam	Silt loam	Silt loam	Silt loam	Loam	Sandy loam
% sand	24.5	24.2	23.6	30.5	48.1	76.5
% silt	64.0	65.0	66.0	57.2	39.2	14.9
% clay	11.5	10.8	10.4	12.3	12.7	8.6
pH	8.3	8.4	8.5	8.5	8.4	8.7
Organic matter (%)	0.17	0.28	0.25	0.22	0.19	0.18
CEC (meq/100 g)	20.9	19.7	19.0	19.3	15.9	10.9
Bulk density (g/cm^3)	1.06	1.06	1.05	1.09	1.17	1.34
Moisture at 1/3 atm (%)	30.0	28.8	28.3	27.0	22.5	12.2

Data were obtained from Table 1, p. 44 of the study report. Textural classifications were confirmed by the reviewer using the NRCS soil texture calculator.

Experimental design: Prior to test substance application, a total of 13 monitoring wells and 56 suction lysimeters were installed at the test site in April 1995 to measure ground water and soil-pore water, respectively (p. 19; Appendix 2, pp. 236-237 and 239). Six clusters consisting of two monitoring wells (one deep well and one shallow well) and eight pressure/vacuum-ceramic cup "suction" lysimeters were installed in the treated plot; one monitoring well and one cluster of suction lysimeters were installed in the control plot. Three clusters were installed in the northern half of the plot and three clusters were installed in the southern half of the plot (placement of instrument clusters is detailed in Appendix 2, Figure 5, p. 307 of the study report). The shallow and deep wells within each cluster had a 10-ft horizontal separation (Appendix 2, Figure 8, p. 310). The 2-inch diameter stainless steel monitoring wells were screened using 0.01-inch slotted screens (Appendix 2, p. 238). In the test plot, shallow wells were installed so that the screened interval (10 ft in length) intersected the top 2-3 feet of ground water surface (*ca*. 15 to 25 ft bgs) and deep wells were installed so that the screened interval (*ca*. 5 ft in length) was positioned immediately below the shallow well screened interval (*ca*. 25 to 30 ft bgs; Appendix 2, p. 237). The control plot contained a single intermediate depth well. Monitoring wells were equipped with a blader pump for sampling (Appendix 2, p. 238; Figures 9-10, pp. 311-312). Lysimeters consisted of a PVC body with a porous ceramic cup at the bottom end to collect soil-pore water from the unsaturated zone (Appendix 2, p. 239). Lysimeters were installed at depths of 3, 6, 9, and 14 feet below ground surface (bgs) in each cluster. The lysimeters were installed *ca*. 18 inches apart in two unplanted instrument rows, having planted rows 30 inches on each side (p. 19; Appendix 2, p. 239). Within each cluster, monitoring wells and lysimeters were installed in line with each other, 18 inches apart (Appendix 2, Figure 8, p. 310).

On June 7, 1995, four days prior to the test application, the site was chisel plowed, disked, planted to corn, and fertilized (p. 29; Appendix 2, p. 241). Wells and lysimeters were covered with plastic sheeting prior to the test application.

Flufenacet (Axiom DF, 54.8% w/w flufenacet, and also containing metribuzin at a concentration of 13.7% w/w) was applied to a 3.0-acre plot at a target rate of 1.01 kg flufenacet/ha, which is equivalent to 0.9 lb flufenacet/A (1.65 lb product/A) on June 11, 1995 (pp. 19-20, 29-30). A conservative ionic tracer, potassium bromide (KBr), was applied at a target application rate of 50 lb KBr/A following the application of the test substance, to monitor the water recharge front (p. 31). The KBr and flufenacet applications were made using a tractor-mounted, boom sprayer equipped with 31 TeeJet Model 8008VS (XR Series) nozzles spaced 20 inches apart. The plot did not receive any rainfall or irrigation until 12 days after the test application (0.32 inches; June 23, 1995), followed by *ca*. 1.3 inches at 17-19 days posttreatment (June 28-30, 1995; Appendix 2, p. 362).

An on-site weather station was installed at the test site, located at the northwest corner of the treated plot, to monitor precipitation/irrigation, air temperature, humidity, solar radiation, wind speed, and direction, soil temperature at 2 and 20 inches, and soil moisture (p. 19; Appendix 2, p. 240). During periods when the data logger failed to record data due to lightning strikes or mechanical failures, supplemental data were obtained from a NOAA weather station located *ca*. 4 miles from the test site (Appendix 2, pp. 256, 536). Soil moisture content was also monitored from three instrument clusters at 1, 3, 6, 9, and 14 feet bgs using soil-moisture probes (p. 19; Appendix 2, pp. 239, 255).

Experimental design.

Details		**Test site**
Duration of study		3102 days (102 months).
Uncropped (bare) or cropped		Bare at application (pre-emergent to corn)
Control used (Yes/No)		Yes
No. of replications	Controls	One
	Treatments	One
Plot size (L x W m)	Controls	105 x 38 m (1.0 acres)
	Treatments	114 x 105 m (3.0 acres)
Distance between control plot and treated plot		15.2 m (hydraulically up-gradient from the treated plot)
Distance between treated plots		N/A
Application rate(s) used (g a.i/ha)		804 g a.i./ha (0.9 lb a.i./A)[1]
Was the maximum label rate per ha used in study? (Yes/No)		No (110% of maximum)[1]
Number of applications		One
Application Date(s) (dd mm yyyy)		11/06/1995
Application method (eg., spraying, broadcast etc.)		Spraying
Type of spray equipment, if used		Tractor-mounted, boom-sprayer equipped with 31 TeeJet Model 8008VS (XR Series) nozzles spaced 20 inches apart.
Total volume of spray solution applied/plot **OR** total amount broadcasted/plot		92.1 gal
Identification and volume of carrier (e.g., water), if used		Water
Name and concentration of co-solvents, adjuvants and/or surfactants, if used		None
Indicate whether the following monthly reports were submitted: Precipitation: Average minimum and maximum air temperature: Average minimum and maximum soil temperature: Average annual frost-free periods:		 No (total water input, rainfall + irrigation was reported). Yes, daily. Yes, daily (at 2 and 20 inches). No
Indicate whether the Pan evaporation data were submitted		Daily evapotranspiration was calculated (Penman equation).
Meteorological conditions during application	Cloud cover	Not reported
	Temperature (°C)	Not reported
	Relative humidity	Not reported
	Wind speed and direction	Not reported
Pesticides used during study: Name of product/a.i conc.: Amount applied: Application method:		Not reported

Details	Test site
Supplemental irrigation used (Yes/No) If yes, provide the following details: No. of irrigation: Interval between irrigation: Amount of water added each time: Method of irrigation:	Yes[2] 17 irrigation events through June 2, 1997 2 days to *ca*. 9 months 0.25-2.75 inches Overhead center pivot system
Indicate whether water received through rainfall + irrigation equals the 30 year average rainfall (Yes/No)	Total water input (precipitation plus irrigation) during the first growing season (June 11-October 31) was 24.76 inches or 128% of the 150% moisture input target. For subsequent years, total water input during the growing season (May 1-October 31) was 20.60, 24.58, 22.87, 34.12, 18.35, 30.70, 45.70, and 20.24 inches, respectively, which equaled 115%, 137%, 128%, 190%, 102%, 171%, 255%, and 113% of the 30-yr average precipitation of 17.93 inches. Total cumulative water input through December 8, 2003 (102 months posttreatment) was 289.62 inches or 139% of the prorated average rainfall of 208.35 inches, not including another 17.70 inches of total water input from snowfall, after conversion.
Were the application concentrations verified?	Yes
Were field spikes used?	No
Good agricultural practices followed (Yes or No)	Not reported
Indicate if any abnormal climatic events occurred during the study (eg., drought, heavy rainfall, flooding, storm etc.)	None reported. The highest water inputs by month were as follows: 14.15 inches - August, 1999 11.90 inches – August, 2002 9.36 inches – June, 2002 8.63 inches – May, 2002 8.49 inches – July, 2002 8.41 inches – August, 1995 7.86 inches – July, 1995 7.51 inches – June, 1999 7.34 inches – July, 2000 7.19 inches – August, 2001 7.06 inches – May, 1996 6.72 inches – July, 1998 6.72 inches – July, 2001 6.63 inches – May, 2003 6.55 inches – July, 1999 6.20 inches – June, 2003 6.14 inches – June, 1997 The largest single input event was 4.88 inches in August 1999.
If cropped plots are used, provide the following details: Plant - Common name/variety: Details of planting: Crop maintenance:	 Corn Planted June 7, 1995, with a row spacing of 30 inches. Three instrument rows were left unplanted to facilitate access to the monitoring equipment. Harvested on November 8, 1995 Dates of planting/harvesting were generally not provided for subsequent years. It was noted that the site was disked in the spring of 2001, 2002, and 2003, and that the site was fertilized with 200 lb of

Details	Test site
	NH_3 in May 2003, and treated with Roundup in June 2003.

Data were obtained from pp. 19-20, 29-30; Tables 2-3, pp. 45-48; and Appendix 2, pp. 232, 240-241, 244-246, 258-259, 362-464, 536; Tables 17-21, pp. 296-301; and Appendix 4, pp. 539-542 of the study report.

1 Values are based on the target application rate. Based on the amount of spray mixture remaining in the tank following the application, the application rate was *ca*. 1.73 lb Axiom DF/A, which is 105% of the targeted amount and 115% of the maximum label rate (p. 30 of the study report).

2 Irrigation applied by the landowner from 1997 through 2004 was not documented (Appendix 2, p. 257 of the study report); however, it was captured by the on-site weather station. It was stated that irrigation was applied at critical crop growth stages to ensure that a commercial yield of field corn was obtained.

Application Verification: To verify the application rate, 15 Petri dishes (3.5-inch diameter) and 15 aluminum trays (14.875 x 10.25 inch) containing a thin layer of sieved (2 mm) control soil were randomly placed together in the treated plot prior to test substance application (three of each were placed in each of the five subplots of the treated plot; p. 20; Appendix 2, p. 246). Immediately after application, the application verification devices were removed from the field, and the soil placed in a cooler with dry ice, then shipped frozen to the analytical laboratory for analysis. Soil from the aluminum pans was homogenized and sub-sampled for analysis, and soil from the Petri dishes was analyzed individually (p. 21). The storage interval of the application monitor samples was not reported.

Field Spiking: Field spikes of soil and ground water samples were not prepared to determine the stability of the parent and the transformation products during transport and storage of the test samples.

Soil sampling: The test plot was divided into five subplots for sampling purposes (p. 20). Twenty-five cores (five from each subplot) were collected from the treated plot to a depth of 12 inches following the test application, and then fifteen soil cores (three from each subplot) were collected to a depth of 1 foot at 1, 3, 8, 15, 29, 57, 93, 181, 286, 374, 468, and 557 days posttreatment (pp. 20, 31; Table 6, p. 51).

Soil sampling.

Details	Treated plot
Method of sampling (random or systematic)	Unknown[1]
Sampling intervals	-18, 0, 1, 3, 8, 15, 29, 57, 93, 181, 286, 374, 468, and 557 days.
Method of soil collection (eg., cores)	Cores were collected using an extendable coring device consisting of a 12-inch stainless steel threaded casing with a cutting head and end cap, and an acetate sleeve.
Sampling depth	30 cm (one foot)
Number of cores collected per plot	Fifteen, excluding day-0 samples in which 25 samples were collected.
Number of segments per core	Two
Length of soil segments (after sectioning)	15 cm
Core diameter	1.75 inches
Method of sample processing, if any	Samples were homogenized by mixing with dry ice and composited by subplot into three samples per depth at each sampling interval.
Storage conditions	Frozen

Storage length	46-175 days

Data were obtained from pp. 20-21, 31, 39, and Appendix 2, p. 248, of the study report.

1 It was stated in Appendix 2 (p. 248) that sampling rows were randomly selected using a random number generator; however, the study deviations section indicated that the numbered grid to be used in conjunction with the random number process appeared to not have been prepared and that the process used was not well documented (Appendix 2, p. 536).

Water sampling: Soil-pore water was collected prior to test treatment, at 9, 16, and 30 days posttreatment, then *ca*. monthly through August 1997 (excluding winter months), and quarterly through 1740 days posttreatment (March 2000) to monitor analyte behavior in the unsaturated zone (p. 31). To monitor the saturated zone, ground water samples were collected prior to test treatment, at 16 and 30 days posttreatment, then *ca*. monthly through June 1997 (741 days posttreatment), and quarterly through 3102 days posttreatment (December 2003). Soil-pore water was collected from lysimeters at depths of 3, 6, 9, and 14 ft below the soil surface using a vacuum applied to each lysimeter for 24-48 hours to draw soil-pore water from the surrounding soil into the reservoir of the lysimeter (p. 20). The collected water was recovered from the reservoir by pressurizing the lysimeter, forcing the water through the Teflon tubing for collection into glass jars. Ground water was collected from shallow and deep wells following purging (minimum of 3 well volumes) using dedicated bladder pumps.

Water sampling.

Details	Soil-pore water	Ground water
Sampling intervals	-1 day, 7 days, 14 days, and at 1, 2, 3, 4, 5, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 21, 22, 23, 24, 26, 29, 32, 35, 38, 41, 46, 48, 51, 54, and 57 months. [1]	-1 day, 14 days, and at 1, 2, 3, 4, 5, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 21, 22, 23, 24, 26, 29, 32, 35, 38, 41, 46, 48, 51, 54, 57, 60, 63, 66, 69, 72, 76, 78, 82, 85, 88, 91, 93, 97, 99, and 102 months.[2]
Method of collection	Collected from lysimeters, which were placed under vacuum *ca*. 24-48 hours before sampling. Within each cluster, samples were collected from the deepest lysimeter first, and the shallowest lysimeter last.	Collected from shallow and deep wells following purging a minimum of 3 well volumes. Samples were collected from deep wells first.
Sampling location	Six lysimeter clusters were installed in the treated plot (three each in the northern and southern halves of the plot).	Six monitoring well clusters were installed in the treated plot (three each in the northern and southern halves of the plot).
Sampling depth	3, 6, 9, and 14 ft below the soil surface.	The shallow well was screened so that its screened interval (10 ft) intersected the top 2-3 feet of ground water surface and deep wells were installed so that its screened interval (*ca*. 5 ft in length) was positioned immediately below the shallow well screened interval.
Number of samples collected per plot	One sample was collected from each lysimeter into a 250-mL amber glass jar, and a *ca*. 4-mL aliquot was removed for bromide analysis.	Two samples were collected from each monitoring well into a 250-mL amber glass jar, with one sample designated for bromide analysis.
Method of sample processing, if any	None reported	None reported

Storage conditions	Placed on ice and shipped on ice to the analytical laboratory. Samples were stored refrigerated at the analytical laboratory prior to analysis.	Placed on ice and shipped on ice to the analytical laboratory. Samples were stored refrigerated at the analytical laboratory prior to analysis.
Storage length	8-185 days	8-200 days through the 1838-day posttreatment sampling interval, then up to 830 days for the remaining sampling intervals.

Data were obtained from pp. 19-21, 39; Table 19, pp. 78-80; Table 32, pp. 123-126; Appendix 2, pp. 249-250, and 274-275; and Figure 5, p. 307 of the study report.

1 Indicates intervals that samples were collected. Additional samples could not be collected at scheduled intervals due to frozen sample delivery lines or unfavorable weather conditions (Appendix 2, p. 247, 534, 537; Appendix 3, p. 538).

2 Some wells were dry and could not be sampled between 88 and 102 months posttreatment (Appendix 2, p. 278).

Analytical Procedures: Soil, lysimeter water, and ground water were analyzed for flufenacet and the transformation products flufenacet alcohol (*N*-(4-fluorophenyl)-2-hydroxy-*N*-(1-methylethyl)acetamide), flufenacet oxalate ([(4-fluorophenyl)(1-methylethyl)]amino-oxoacetic acid), flufenacet sulfonic acid (4-fluoro-*N*-methylethylaniline-sulfoacetamide), and flufenacet thiadone (3-trifluoromethyl-1,3,4-thiadiazol-2(3*H*)one; pp. 22-26; Figure 1, pp. 127-128).

Extraction, clean up and concentration of soil samples: Soil samples (10 g) were extracted by shaking for one hour with 20 mL of acetonitrile:0.1N HCl (1:1, v:v), and centrifuged for 10 minutes (p. 22). A 10-mL aliquot was then combined with *ca*. 1 mL of methanol and an internal standard solution containing isotopically labeled standards for each analyte. The sample was evaporated to *ca*. 4.9 mL and then adjusted to 5 mL with 0.1% formic acid. An aliquot of the extract was filtered (0.45 µm) prior to analysis.

Extraction, clean up and concentration of water samples: Water samples (50-mL aliquots) were acidified with 10 mL of 1N HCl, fortified with an internal standard solution, and passed through a octadecyl (C18) Solid Phase Extraction (SPE) column (p. 24). The analytes were eluted with 6 mL of methanol and concentrated to *ca*. 1 mL using nitrogen and a water bath at 25-30°C. The concentrate was brought to 2 mL with 0.1% formic acid and syringe filtered (0.45 µm) prior to analysis.

Identification and quantification of parent compound and transformation products in soil and water samples: Flufenacet and the transformation product flufenacet alcohol were analyzed by HPLC (Inertsil ODS-2 column, 50 x 3 mm; 5 µm) with a mobile phase gradient of 0.1% formic acid:0.1% formic acid in acetonitrile (90:10 to 10:90 to 90:10, v:v) and a Finnigan TSQ 7000 Mass Spectrometer (for soil samples) or a Sciex API III Mass Spectrometer (for water samples) operated in the positive ion mode (pp. 22, 24-25). A second aliquot of the extract was analyzed for flufenacet oxalate, flufenacet sulfonic acid, and flufenacet thiadone by HPLC (Inertsil ODS-2 column, 50 x 3 mm; 5 µm) with a mobile phase gradient of 0.1% formic acid:0.1% formic acid in acetonitrile (90:10 to 30:70 to 90:10, v:v) and a Finnigan TSQ 7000 Mass Spectrometer (for soil samples) or a Sciex API III Mass Spectrometer (for water samples) operated in the negative ion mode.

Reference standards.

Compound	Reference No.	Purity
Flufenacet	K-597	99.6%
Flufenacet alcohol	K-449	99.1%
Flufenacet oxalate	K-596	99.2%
Flufenacet sulfonic acid	K-534	98.5%
Flufenacet thiadone	K-510	99.6%

Data were obtained from pp. 127-128 of the study report.

Detection limits (LOD, LOQ) for the parent compound and transformation products in soil: The LOQ was 10 µg/kg for each analyte (p. 22). The Method Detection Limit (MDL) was 1.8 µg/kg for flufenacet, 1.7 µg/kg for flufenacet alcohol, 1.7 µg/kg for flufenacet oxalate, 2.5 µg/kg for flufenacet sulfonic acid, and 1.3 µg/kg for flufenacet thiadone (p. 34).

Detection limits (LOD, LOQ) for the parent compound and transformation products in water: The LOQ was 0.1 µg/L for each analyte (p. 24). The MDL was 0.012 µg/L for flufenacet, 0.010 µg/L for flufenacet alcohol, 0.015 µg/L for flufenacet oxalate, 0.008 µg/L for flufenacet sulfonic acid, and 0.024 µg/L for flufenacet thiadone (p. 36).

Soil, soil-pore water, and ground water were also analyzed for the bromide tracer based on the method of Varma, which involves the oxidation of bromide to bromine with 2-iodosobenzoate, followed by reaction of bromine with 2,6-dimethylphenol to form 4-bromo-2,6-dimethylphenol (4-BDMP), which is then analyzed by reverse-phase HPLC with UV detection (pp. 26-28). The LOQ for bromide in soil was 0.1 mg/kg, and the LOQ for bromide in water was 0.1 mg/L (p. 26; Tables 5, 12 and 26, pp. 50, 57, and 99).

Storage stability: Aliquots of pooled soil-pore water and ground water samples were fortified at 1 µg/L with a mixed standard of flufenacet, flufenacet alcohol, flufenacet oxalate, flufenacet sulfonic acid, and flufenacet thiadone and analyzed following 0, 30, 90, and 194 days of refrigerated storage (pp. 39-40). Recoveries of each analyte from fortified water samples did not exhibit a pattern of decline through the 194-day storage interval; however, flufenacet residues declined to 74% at the 194-day interval, but too few sampling intervals were employed to distinguish a pattern of decline. The storage interval covered the longest storage interval for the test samples with the exception of seven ground water sampling intervals (1838, 1937, 2210, 2574, 2747, 2940, and 3102 days; Table 32, pp. 123-126).

Recovery from storage stability samples

Interval (days)	Water sample	Percent recovery				
		Flufenacet	Flufenacet sulfonic acid	Flufenacet oxalate	Flufenacet thiadone	Flufenacet alcohol
0	Soil-pore	109	108	111	107	98
30	Soil-pore	102	106	112	106	98
90	Soil-pore	107	117	119	109	97
194	Soil-pore	105	119	121	111	93
0	Well	107	108	113	106	98
30	Well	102	104	108	103	96
90	Well	105	113	116	104	94
194	Well	74	118	126	139	101

The study authors reported that flufenacet, flufenacet oxalate, flufenacet sulfonic acid, and flufenacet alcohol were stable in soil stored frozen for up to 24 months, and that flufenacet thiadone had a storage half-life of 725 days (losses were reportedly due to carbon dioxide formation in the head space of the jars; p. 40). Details of the study and individual recoveries were not provided. The 24-month storage interval exceeds the longest storage interval for the test samples.

RESULTS AND DISCUSSION

Meteorological conditions during the study: Total water input during the first growing season (June 11-October 31) was 24.76 inches or 128% of the 150% moisture input target (Appendix 2, p. 258). For subsequent years, total water input during the growing season (May 1-October 31) was 20.60, 24.58, 22.87, 34.12, 18.35, 30.70, 45.70, and 20.24 inches, respectively, which equaled 115%, 137%, 128%, 190%, 102%, 171%, 255%, and 113% of the 30-yr average precipitation of 17.93 inches. Total cumulative water input through December 8, 2003 (102 months posttreatment), was 289.62 inches or 139% of the prorated average rainfall of 208.35 inches (Figure 3, p. 130; Appendix 2, p. 259; Table 18, pp. 297-299). An additional 177.0 inches of snowfall occurred during the study period, which is equivalent to 17.70 inches of water (Appendix 2, Tables 19-20, p. 300). The highest single water input event and monthly water totals were 4.88 and 14.15 inches, respectively, both occurring in August 1999 (Appendix 2, pp. 362-464).

Site hydrology during the study: The mean saturated zone hydraulic conductivity at the site was 1.8 ft/day (range from 0.55 to 2.58 ft/day), determined from rising head slug tests performed in three monitoring wells (p. 29; Appendix 2, pp. 252-253; Table 13, p. 281). The depth to ground water ranged from 20.6 to 33.3 ft bgs and showed a seasonal variation, with the deepest levels observed in the final months of the study (p. 29; Appendix 2, p. 253; Table 14, pp. 282-293 and Figure 16, p. 321). The ground water flow direction was predominantly to the northeast, with an average flow velocity of 1.36×10^{-2} ft/day (range from 3.0×10^{-3} to 2.7×10^{-2} ft/day; Appendix 2, pp. 254-255; Table 15, p. 294; Figure E1-E47, pp. 483-529). Porosity was estimated at 38% (Appendix 2, p. 255). Soil moisture data, collected from three locations, indicated a spatially homogeneous soil moisture profile across the test plot (Appendix 2, p. 255; Table 16, p. 295).

Application monitors: Mean recovery of flufenacet from the Petri dishes was 114% of the label rate, and mean recovery of flufenacet from the aluminum trays was 112% of the label rate. (p. 30).

The KBr application was not verified using application monitoring devices. However, analysis of post-application soil cores indicated a KBr application rate of 31.2 lb/A (62% of the target application rate; p. 31).

Mean concentration of flufenacet residues expressed as ppb soil, at the test site.

Compound	Soil depth (cm)	Sampling times (days)											
		0	**1**	**3**	**8**	**15**	**29**	**57**	**93**	**181**	**286**	**374**	**468**
Flufenacet	0-15	370	523	410	400	320	220	44	25	12	(9)	(8)	(4)
	15-30	<MDL	(4)	(3)	10	(7)	(1)	<MDL	3	<MDL	<MDL	<MDL	<MDL
Flufenacet Alcohol	0-15	<MDL	<MDL[1]	<MDL	<MDL[1]	<MDL[1]	(2)	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
	15-30	<MDL	<MDL	<MDL	<MDL[1]	<MDL[1]	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
Flufenacet Oxalate	0-15	<MDL	<MDL	<MDL	<MDL	(2)	10	(3)	<MDL	<MDL	<MDL	<MDL	<MDL
	15-30	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	(2)	<MDL	<MDL	<MDL	<MDL	<MDL
Flufenacet Sulfonic acid	0-15	<MDL	<MDL	<MDL	<MDL	<MDL	10	(6)	<MDL[1]	<MDL	(3)	<MDL	<MDL
	15-30	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	(5)	(3)	<MDL	<MDL	<MDL	<MDL
Flufenacet Thiadone	0-15	(3)	(3)	(3)	(3)	(4)	(5)	(3)	<MDL[1]	<MDL[1]	<MDL	<MDL	<MDL
	15-30	<MDL	<MDL	<MDL	<MDL[1]	<MDL	<MDL	<MDL[1]	<MDL	<MDL	<MDL	<MDL	<MDL

Data were obtained from Tables 6-10, pp. 51-55 of the study report. Mean values for day-0 are the mean of 25 individual samples, and mean values for all other sampling intervals are means of the three composite samples. Values in parenthesis are between the LOD and LOQ (10 ppb for each analyte).

1 Mean concentration was <MDL (Method Detection Limit); however, the maximum replicate concentration was between the LOD and LOQ.

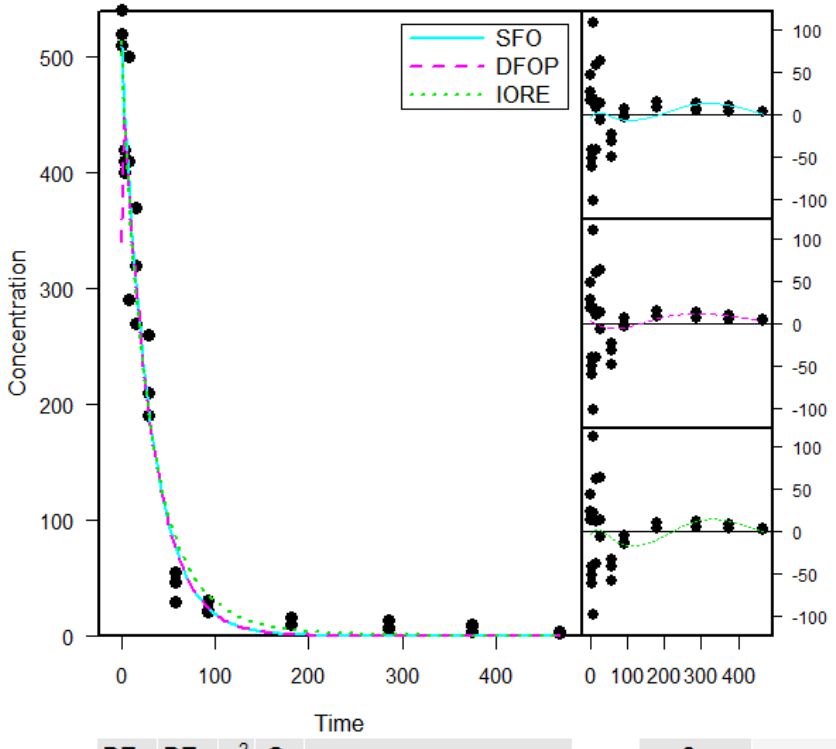
Soil: The mean measured concentration of **flufenacet** in the 0-15 cm soil depth was a maximum of 523 ppb at 1 day, which is *ca*. 80% of the theoretical (reviewer-calculated) and decreased to 320 ppb by 15 days, 220 ppb by 29 days, 44 ppb by 57 days, and declined to <LOQ by 468 days posttreatment (Table 6, p. 51). Flufenacet was only detected at a mean concentration above the LOQ once in the 15-30 cm depth, at 10 ppb at 8 days posttreatment. Soil samples were not collected below 30 cm. The transformation products flufenacet alcohol, flufenacet oxalate, flufenacet sulfonic acid, and flufenacet thiadone were all detected at low levels (<LOQ) in the top 0-15 cm soil depth, with only flufenacet oxalate and flufenacet sulfonic acid detected at a mean concentration above the LOQ (both detected at 10 ppb at 29 days; Tables 7-10, pp. 52-54). Transformation products were not detected in soil following 286 days posttreatment.

The **bromide tracer** passed into the 15-30 cm soil depth between 15 and 29 days posttreatment, which is to be expected since the site did not receive significant water input from rainfall or irrigation until 17 days posttreatment (p. 33; Table 5, p. 50; Figure 5, p. 132).

Flufenacet had a DT_{50} value of 21.1 days in soil, calculated from the 0-15 cm soil residue data following the maximum detection at 1 day posttreatment (single first order model; see Table below).

Dissipation of flufenacet from soil (0-15 cm)

Days Posttreatment	Flufenacet (ppb)
1	510.
1	540.
1	520.
3	420.
3	410.
3	400.
8	290.
8	500.
8	410.
15	270.
15	370.
15	320.
29	210.
29	260.
29	190.
57	55.0
57	47.0
57	29.0
93	31.0
93	21.0
93	22.0
181	16.0
181	10.0
181	10.0
286	6.00
286	13.0
286	7.00
374	10.0
374	9.00
374	4.00
468	3.00
468	4.00
468	4.00



	DT_{50}	DT_{90}	χ^2	C_0	Parameters
SFO	21.1	70.1	10	509	k = 0.0328
DFOP	33.4	82.4	11	340	f = 1.5, k_0 = 0.0328, k_1 = 17.7
IORE	20.5	77.4	11	513	N = 1.15, k = 0.0138

S_C	5.45e+04
S_{SFO}	4.82e+04
Slow $t_{1/2}$	21.1
$t_{R\ IORE}$	23.3

Output from R Version 2.15. Kinetics models: Single First-Order (SFO); Double First-Order in Parallel (DFOP), and Indeterminate Order Rate Equation (IORE).

Soil-pore water: Flufenacet was detected in only 1 of 610 soil-pore water samples, at a level below the LOQ at 30 days (6-ft depth; pp. 36-37; Table 14, pp. 63-65). Flufenacet sulfonic acid was the most prevalent transformation product detected in soil-pore water samples, detected in 104 of 610 samples. Flufenacet sulfonic acid was first detected in soil-pore water at 58 days (3-, 6-, and 9-ft depths; *ca*. 1 month following detection of the Br tracer), was a maximum of 5.20 ppb in the 3-ft depth (at 119 days), 3.80 ppb in the 6-ft depth (at 412 days), 1.00 ppb in the 9-ft depth (at 94 days), and 1.40 ppb in the 14-ft depth (at 897 days; Table 17, pp. 72-74). Flufenacet oxalate was detected in 22 of 610 samples, and at a maximum of 0.33 ppb in the 9-ft depth at 94 days (Table 16, pp. 69-71). Residues declined to background by 665 days and 1254 days for flufenacet oxalate and flufenacet sulfonic acid, respectively. Flufenacet alcohol and flufenacet thiadone were generally not detected in soil-pore water, with only 2-5 detections each, at levels below the LOQ, out of 610 samples analyzed (Tables 15 and 18, pp. 66-68 and 75-77). Total flufenacet residues were greatest in the 3- and 6-ft depths (Figure 26, p. 153); residue levels varied considerably between the six instrument clusters (Figure 27, p. 154).

The **bromide tracer** was first observed in the 3-, 6- and 9-ft lysimeters at 30 days posttreatment and in the 14-ft lysimeter at 94 days posttreatment (p. 35; Tables 12-13, pp. 57-62 and Figures 20-21, pp. 147-148). Mean Br levels in soil-pore water were a maximum of 1.41 ppm in the 3-ft lysimeter (at 119 days), 1.28 ppm in the 6-ft lysimeter (at 468 days), 1.11 ppm in the 9-ft lysimeter (at 665 days), and 1.51 ppm in the 14-ft lysimeter (at 897 days), with concentrations decreasing to background levels at the 3-, 6-, and 9-ft depths by the end of the study period, and to a mean of 0.14 ppm in the 14-ft lysimeter by 1740 days posttreatment.

Maximum flufenacet concentrations, ppb, in soil-pore water.

Compound	Depth	Days posttreatment															
		9	**16**	**30**	**58**	**94**	**119**	**151**	**286**	**313**	**342**	**375**	**412**	**438**	**468**	**503**	**533**
Flufenacet	3– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	6– ft	nd	nd	(0.02)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	9– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	14– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Alcohol	3– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	6– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	9– ft	nd	nd	nd	nd	(0.02)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	14– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Oxalate	3– ft	nd	nd	nd	nd	nd	(0.06)	(0.04)	nd	nd	nd	(0.02)	(0.02)	nd	nd	nd	nd
	6– ft	nd	nd	nd	0.23	nd	nd	nd	nd	nd	nd	nd	(0.08)	0.12	nd	nd	nd
	9– ft	nd	nd	nd	0.23	0.33	(0.07)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	14– ft	nd	nd	nd	nd	(0.06)	(0.05)	(0.04)	nd	nd	nd	nd	(0.04)	(0.07)	0.14	0.15	(0.08)
Flufenacet Sulfonic acid	3– ft	nd	nd	nd	0.52	1.40	5.20	2.60	nd	0.57	0.28	0.11	(0.02)	(0.04)	nd	nd	(0.01)
	6– ft	nd	nd	nd	0.61	0.22	(0.03)	(0.03)	(0.07)	1.20	2.20	0.14	3.80	3.60	0.14	0.28	(0.01)
	9– ft	nd	nd	nd	0.25	1.00	0.24	(0.04)	0.22	0.25	0.24	(0.06)	(0.08)	(0.04)	0.11	0.19	0.23
	14– ft	nd	nd	nd	nd	0.29	0.45	0.39	0.15	0.13	nd	(0.05)	(0.03)	0.13	0.39	0.57	0.62
Flufenacet Thiadone	3– ft	nd	nd	nd	(0.09)	(0.07)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	6– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	9– ft	nd	nd	nd	nd	(0.04)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	14– ft	nd	nd	nd	nd	nd	nd	(0.03)	nd	nd	nd	(0.03)	nd	nd	nd	nd	nd

Data were obtained from Tables 14-25, pp. 63-98 in the study report. Values in parenthesis are between the LOD and LOQ (0.1 µg/L). nd = Not detected (<MDL).

Maximum flufenacet concentrations, ppb, in soil-pore water (continued).

Compound	Depth	Days posttreatment															
		559	**665**	**693**	**715**	**741**	**805**	**897**	**996**	**1061**	**1155**	**1254**	**1416**	**1474**	**1566**	**1645**	**1740**
Flufenacet	3– ft	nd	nd	nd	ns	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	6– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	9– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	14– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	na
Flufenacet Alcohol	3– ft	nd	nd	nd	ns	nd	nd	nd	ns	nd	nd	(0.01)	nd	nd	nd	nd	na
	6– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	9– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	14– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	na
Flufenacet Oxalate	3– ft	nd	nd	nd	ns	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	6– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	9– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	14– ft	(0.06)	nd	nd	nd	(0.02)	nd	nd	nd	nd	nd	nd	nd	(0.03)	nd	nd	na
Flufenacet Sulfonic acid	3– ft	nd	nd	nd	ns	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	6– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	9– ft	0.27	0.24	0.22	0.24	0.21	0.18	(0.03)	ns	nd	nd	nd	nd	nd	nd	nd	na
	14– ft	0.65	0.44	0.39	0.35	0.29	0.28	1.40	0.43	0.55	0.11	nd	nd	nd	nd	nd	na
Flufenacet Thiadone	3– ft	nd	nd	nd	ns	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	6– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	9– ft	nd	nd	nd	nd	nd	nd	nd	ns	nd	nd	nd	nd	nd	nd	nd	na
	14– ft	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	na

Data were obtained from Tables 14-25, pp. 63-98 in the study report. Values in parenthesis are between the LOD and LOQ (0.1 µg/L). nd = Not detected (<MDL). ns = No sample. na = Not analyzed.

Ground water: Flufenacet was not detected in shallow or deep ground water samples, excluding one detection below the LOQ prior to breakthrough of the tracer (Table 27, pp. 103-106). Flufenacet sulfonic acid was the most prevalent transformation product detected in ground water samples, detected in 107 of 482 samples (p. 38; Table 30, pp. 115-118). Flufenacet sulfonic acid was first detected in the shallow ground water in the southeast cluster at the LOQ at 93 days, and did not appear in another cluster at a level above the LOQ until 1061 days and 1644 days when it appeared in the south central and northeast clusters, respectively. Flufenacet sulfonic acid residues peaked in the shallow ground water of the southeast cluster at 0.66 ppb at 501-534 days, then declined to <LOQ by 895 days. Flufenacet sulfonic acid residues did not peak in the shallow ground water samples from the south central and northeast clusters until 1155 days and 2210 days, respectively. Flufenacet sulfonic acid first appeared above background levels in the deep ground water samples, southeast cluster only, at 149 days, was first detected above the LOQ at 412 days, increased to a maximum of 0.27-0.28 ppb by 534-664 days, then declined to <LOQ by 994 days posttreatment. Flufenacet sulfonic acid first appeared in the south central and northeast clusters, above background levels, at 805 days and 1565 days, respectively, with maximums of 0.23 ppb in the south central cluster at 1412 days and 0.27 ppb in the northeast cluster at 2299 days. Flufenacet thiadone was detected in 39 of 482 ground water samples (p. 38; Table 31, pp. 119-122). Residues of flufenacet thiadone reached shallow wells by 119 days and deep wells by 412 days posttreatment, then declined to background levels by 1155 days for shallow wells and 895 days for deep wells; detections were generally limited to the southeast and south central clusters. Maximum flufenacet thiadone residues were 0.18 ppb for shallow wells (at 501 days) and near the LOQ for deep wells (at 664 days). Flufenacet oxalate was not detected above the LOQ in shallow and deep ground water samples, excluding one exception near the LOQ (0.12 ppb in the shallow well at 149 days), and flufenacet alcohol was only detected in one ground water sample, at a level below the LOQ (Tables 28, pp. 107-110). Flufenacet and its transformation products were not detected in ground water samples from the control plot, excluding a few sporadic detections near the MDL.

Excluding one outlier, the **bromide tracer** was initially detected in the shallow ground water well from the southeast cluster (MWSE) at 119 days posttreatment and first appeared consistently in the deep monitoring well at that cluster at 375 days (p. 37, Table 26, pp. 99-102; Figures 37-38, pp. 182-183). The tracer did not appear in shallow wells at the other five instrument clusters until 994-1565 days posttreatment, and did not appear consistently in the deep wells until 1155-2021 days. Mean Br levels in ground water were a maximum of 1.36 ppm in the shallow monitoring wells at 1838 days and 1.05 ppm in the deep monitoring wells at 2021 days posttreatment. Br levels dropped to a mean of 0.84 ppm by 2574 days, which was the last interval that shallow wells could be sampled because the water table depth dropped below the pump intake. Br was detected in 5 of the 6 deep monitoring wells at the end of the study period, 3102 days, at levels ranging from 0.49 to 2.25 ppm (mean of 0.91 ppm).

Maximum flufenacet concentrations, ppb, in ground water.

Compound	Depth	Days posttreatment													
		16	**30**	**58**	**93**	**119**	**149**	**286**	**312**	**340**	**375**	**412**	**438**	**469**	**501**
Flufenacet	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	Deep	nd	(0.04)	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Alcohol	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Oxalate	Shallow	nd	nd	nd	(0.06)	(0.09)	0.12	(0.05)	(0.06)	(0.03)	nd	(0.03)	nd	(0.05)	(0.06)
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Sulfonic acid	Shallow	nd	nd	nd	0.10	0.13	0.21	0.15	0.24	0.11	0.19	0.37	0.52	0.56	0.66
	Deep	nd	nd	nd	nd	nd	(0.02)	(0.07)	(0.08)	(0.08)	(0.09)	0.12	0.16	0.21	0.24
Flufenacet Thiadone	Shallow	nd	nd	nd	nd	(0.04)	(0.06)	(0.07)	0.10	nd	(0.08)	0.10	0.13	0.16	0.18
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	(0.06)	(0.05)	(0.06)	(0.09)
		Days posttreatment													
		534	**558**	**664**	**692**	**713**	**741**	**805**	**895**	**994**	**1061**	**1155**	**1254**	**1412**	**1473**
Flufenacet	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Alcohol	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	(0.02)	nd	nd	nd	nd	nd
Flufenacet Oxalate	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	(0.02)	nd
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Sulfonic acid	Shallow	0.66	0.59	0.34	0.28	0.29	0.24	0.15	(0.06)	(0.07)	0.34	0.80	0.58	0.40	0.37
	Deep	0.28	0.28	0.27	0.19	0.16	0.12	0.16	0.30	(0.03)	nd	(0.09)	0.20	0.23	0.22
Flufenacet Thiadone	Shallow	0.12	0.17	0.14	0.10	0.13	0.12	(0.09)	(0.03)	(0.03)	(0.03)	nd	nd	nd	nd
	Deep	(0.08)	(0.08)	(0.09)	(0.08)	(0.07)	(0.06)	(0.03)	nd	nd	nd	nd	nd	nd	nd
		Days posttreatment													
		1565	**1644**	**1740**	**1838**	**1937**	**2021**	**2119**	**2210**	**2299**	**2383**	**2574**	**2747**	**2940**	**3102**
Flufenacet	Shallow	nd	nd	nd	nd	nd	nd	nd	ns	ns	ns	nd	nd[1]	ns	ns
	Deep	nd	nd	nd	nd	nd	nd	nd	ns	ns	ns	nd	nd	nd	nd
Flufenacet Alcohol	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd[1]	ns	ns
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Oxalate	Shallow	nd	nd	nd	nd	nd	nd	nd	(0.04)	(0.03)	(0.02)	nd	nd[1]	ns	ns
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Flufenacet Sulfonic acid	Shallow	(0.09)	0.18	0.24	0.52	0.39	0.43	0.60	1.60	1.30	0.60	0.30	nd[1]	ns	ns
	Deep	0.19	0.15	0.15	0.15	0.15	0.10	(0.05)	0.15	0.27	0.14	(0.08)	(0.07)	(0.09)	(0.07)
Flufenacet Thiadone	Shallow	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd[1]	ns	ns
	Deep	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	(0.03)	(0.04)	(0.05)	(0.03)

Data were obtained from Tables 27-31, pp. 103-122 in the study report. Values in parenthesis are between the LOD and LOQ (0.1 µg/L). nd = Not detected (<MDL). ns = No sample.
1 Five of six clusters could not be sampled.

STUDY DEFICIENCIES:

1. The test site did not receive adequate water input during the initial month of the study. EPA Guidance states that the initial irrigation event should be a minimum of 1.0 inches and scheduled to occur within three days after the pesticide application, and that the first month's targeted rainfall plus irrigation amounts should be divided into four periods of 7-8 days each, and at least one fourth of the target monthly water requirement should occur in each of the four periods. The plot did not receive any rainfall or irrigation until 12 days after the test application (0.32 inches; June 23, 1995), followed by *ca*. 1.3 inches at 17-19 days posttreatment (June 28-30, 1995; Appendix 2, p. 362). The reviewer does not consider this a major guideline deficiency since the total water input was 128% of the 150% moisture input target for the first growing season and total water input greatly exceeded historical precipitation (139%) during the entire study period. Additional water input may have shortened the study period. However, the reviewer notes that the study was conducted until Br levels peaked and that residues of the flufenacet transformation products peaked and declined in ground water. Flufenacet appeared to dissipate completely prior to reaching ground water.

2. The stability of flufenacet and its transformation products in ground water samples was not properly demonstrated. Well water samples were analyzed following up to 194 days of refrigerated storage (p. 40); however, test samples were stored for 200-830 days prior to analysis at seven ground water sampling intervals towards the end of the study (1838, 1937, 2210, 2574, 2747, 2940 and 3102 days; Table 32, pp. 123-126). The reviewer notes that recovery of flufenacet declined from 102-107% from 0-90 days to 74% following 194 days of storage, and that more intervals are necessary to determine if the observed decline is the beginning of a pattern. Storage stability studies must be conducted for a length of time at least as long as the longest interval for the test samples to demonstrate stability during the storage period.

3. The plot use history was not provided to allow the reviewer to determine whether similar chemicals were applied to the plot within the prior five years or during the study period that could have affected the interpretation of study results or interfere with the analytical procedures (Appendix 2, p. 536). All pesticide use during the study and for five years prior should be documented, as well as agronomic practices used during the study period (including planting and harvesting dates).

REVIEWER'S COMMENTS:

1. An irrigation well was installed in May 1994, *ca*. 110 ft northeast of the test plot and screened at 120-140 feet bgs (p. 29). The study authors stated that the well was not expected to have an impact on the depth or flow direction of ground water at the test site due to the depth of the screened interval, low pumping rate (120 gallons/minute), and distance from the test site. Study sites should not be located within the radius of influence

or irrigation or production wells. EPA guidance states that if the irrigation source is a well within a quarter mile of the test plot, then the effect of pumping should be determined by using a data logger in the monitoring well nearest the irrigation well and monitoring any drawdown of the depth of water when the irrigation well pump is turned on.

2. Hydraulic conductivity of the saturated soils below the water table was determined using rising head slug tests in three monitoring wells within the test plot (p. 18). EPA guidance recommends that hydraulic conductivity be measured in every well because slug tests sample only a very small region around the well (a minimum of six locations).

3. EPA Guidance states that candidate sites for a prospective ground water study should be of a single soil series mapping unit to minimize site variability. The study site was predominantly a Coly-Kenesaw silt loam and also contains Hobbs silt loam (Appendix 2, Figure 4, p. 306). Additionally, soil characterization was determined from four boreholes at the corners of the test plot and from two additional locations (Appendix 2, pp. 233-234; Tables 2-3, pp. 265-269). EPA guidance requires collection of at least eight cores to assess the vertical and horizontal homogeneity of the soil across the study site.

4. Six clusters consisting of two monitoring wells (one deep well and one shallow well) were established in the test plot rather than the minimum of eight monitoring well locations, as specified in the 2008 EPA Guidance document for prospective ground water monitoring studies.

5. Mass balances were not determined. EPA guidance states that a mass balance for the conservative tracer and pesticide residues should be reported for each instrument cluster.

6. Recoveries from control soil samples fortified at 100 µg/kg and analyzed with each analytical set were 87.8 ± 4.1% for flufenacet, 91.0 ± 10.6% for flufenacet alcohol, 93.7 ± 4.4% for flufenacet oxalate, 81.5 ± 12.4% for flufenacet sulfonic acid, and 94.5 ± 5.1% for flufenacet thiadone (p. 34).

7. Recoveries from control soil-pore water samples fortified at 1.0 µg/L and analyzed with each analytical set were 100 ± 7% for flufenacet, 98 ± 5% for flufenacet alcohol, 99 ± 5% for flufenacet oxalate, 100 ± 5% for flufenacet sulfonic acid, and 100 ± 4% for flufenacet thiadone (p. 36).

8. Recoveries from control ground water samples fortified at 1.0 µg/L and analyzed with each analytical set were 101 ± 7% for flufenacet, 97 ± 5% for flufenacet alcohol, 100 ± 4% for flufenacet oxalate, 99 ± 4% for flufenacet sulfonic acid, and 98 ± 5% for flufenacet thiadone (p. 38).

9. An independent laboratory method validation was not conducted. A method validation study should be completed separate from and prior to the analysis of the test samples to verify the analytical methods.

10. The soil method was reportedly validated for flufenacet and its transformation products by fortifying samples at 10, 20, and 50 µg/kg (pp. 33-34). Mean recoveries were 94.2 ± 5.4% for flufenacet, 81.0 ± 2.3% for flufenacet alcohol, 93.5 ± 5.9% for flufenacet oxalate, 86.9 ± 6.3% for flufenacet sulfonic acid, and 92.8 ± 6.3% for flufenacet thiadone.

11. The water method was reportedly validated for flufenacet and its transformation products by fortifying samples from the test site at 0.1, 0.2 and 0.5 µg/L (p. 36). Mean recoveries were 96 ± 4.1% for flufenacet, 95 ± 3.0% for flufenacet alcohol, 95 ± 6.5% for flufenacet oxalate, 97 ± 5.8% for flufenacet thiadone, and 99 ± 4.4% for flufenacet sulfonic acid.

12. The study author reported a half-life value for flufenacet of 20.4 days ($r^2 = 0.93$) using simple first-order kinetics (p. 35).

13. A detailed description of the installation of the monitoring wells was provided in Appendix 2 of the study report (pp. 326-359).

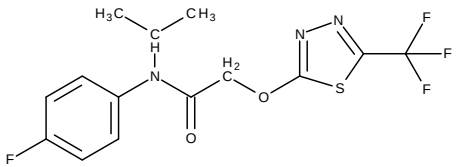
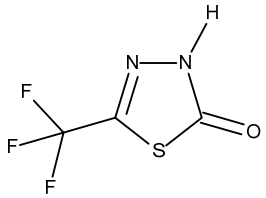
14. Ground water pH values ranged from 6.67 to 7.60 standard units in the shallow and deep monitoring wells, excluding high readings of 8.24-8.29 in the shallow and deep wells at 22 months posttreatment (May 3, 1997; Appendix 2, p. 251; Table 12, pp. 279-280; Figure 14, pp. 317-318).

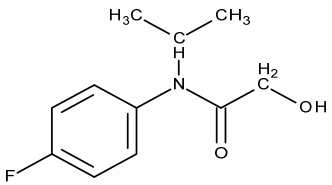
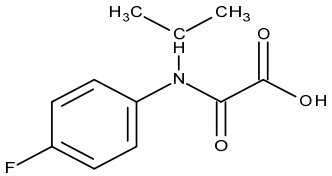
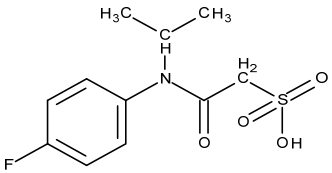
15. A companion ground water monitoring study was conducted in Iowa to evaluate the use of flufenacet on a vulnerable soil (Bayer Study No. F3212401; p. 14).

REFERENCES:

1. U.S. Environmental Protection Agency. 2008. Guidance for Prospective Ground-Water Monitoring Studies.

DER ATTACHMENT 1. Flufenacet and Its Environmental Transformation Products. [A]

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
PARENT						
Flufenacet (FOE 5043)	**IUPAC:** 4'-Fluoro-N-isopropyl-2-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yloxy]acetanilide **CAS:** N-(4-fluorophenyl)-N-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]acetamide **CAS No.:** 142459-58-3 **Formula:** $C_{14}H_{13}F_4N_3O_2S$ **MW:** 363 g/mol **SMILES:** CC(C)N(c1ccc(cc1)F)C(=O)COc2nnc(s2)C(F)(F)F		835.7100 Ground water	46997402	--	--
TRANSFORMATION PRODUCTS						
Thiadone	**IUPAC:** N-(5-trifluoromethyl-1,3,4-thiadiazol-2(3H)one **CAS:** 1,3,4-Thiadiazol-2(3H)one, 5-(trifluoromethyl)- **CAS No.:** 84352-75-0 **Formula:** $C_3HF_3N_2OS$ **MW:** 170 g/mol **SMILES:** c1(n[nH]c(=O)s1)C(F)(F)F		835.7100 Ground water	46997402	--	--

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
Alcohol	**CAS:** N-(4-fluorophenyl)-2-hydroxy-N-(1-methyl-ethyl)acetamide **Formula:** $C_{11}H_{14}FNO_2$ **MW:** 211 g/mol **SMILES:** CC(C)N(c1ccc(cc1)F)C(=O)CO		835.7100 Ground water	46997402	--	--
Oxalate	**CAS:** [(4-Fluorophenyl) (1-methylethyl)amino]oxoacetic acid **Formula:** $C_{11}H_{12}FNO_3$ **MW:** 225 g/mol **SMILES:** CC(C)N(c1ccc(cc1)F)C(=O)C(=O)O		835.7100 Ground water	46997402	--	--
Sulfonic acid	**CAS:** 2-(4-Fluoro-N-isopropyl-anilino)-2-oxo-ethanesulfonic acid **Formula:** $C_{11}H_{14}FNO_4S$ **MW:** 275 g/mol **SMILES:** CC(C)N(c1ccc(cc1)F)C(=O)CS(=O)(=O)O		835.7100 Ground water	46997402	--	--

Attachment 2: Statistics Spreadsheets and Graphs

Attachment 3: Calculations

Calculations were performed by the reviewer using R software, and the following equations.

Single First-Order (SFO) Model

$$C_t = C_0 e^{-kt} \quad \text{(eq. 1)}$$

where,

C_t = concentration at time t (%)
C_0 = initial concentration (%)
e = Euler's number (-)
k = SFO rate constant of decline (d^{-1})
t = time (d)

The SFO equation is solved with R kinetics software by adjusting C_0 and k to minimize the objective function (S_{SFO}) shown in equation 9.

DT_{50} = natural log (2)/k (eq. 2)

DT_{90} = ln (10)/k (eq. 3)

Indeterminate Order Rate Equation (IORE) Model

$$C_t = \left[C_0^{(1-N)} - (1-N)k_{IORE}t\right]^{\left(\frac{1}{1-N}\right)} \quad \text{(eq. 4)}$$

where,

N = order of decline rate (-)
k_{IORE} = IORE rate constant of decline (d^{-1})

This equation is solved with R kinetics software by adjusting C0, kIORE, and N to minimize the objective function for IORE (SIORE) (See equation 9). Half-lives for the IORE model are calculated using equation 5, which represents a first-order half-life that passes through the DT_{90} of the IORE model. (Traditional DT_{50} and DT_{90} values for the IORE model can be calculated using equations 6 and 7.)

$$t_{IORE} = \frac{\log(2)}{\log(10)} \frac{C_0^{1-N}\left(1 - 0.1^{(1-N)}\right)}{(1-N)k_{IORE}} \quad \text{(eq. 5)}$$

$$DT_{50} = \frac{(C_0/2)^{(1-N)} - C_0^{(1-N)}}{k(N-1)} \quad \text{(eq. 6)}$$

$$DT_{90} = \frac{(C_0/10)^{(1-N)} - C_0^{(1-N)}}{k(N-1)} \quad \text{(eq. 7)}$$

Double First-Order in Parallel (DFOP) Model

$$C_t = C_0 g e^{-k_1 t} + C_0 (1-g) e^{-k_2 t} \quad \text{(eq. 8)}$$

where,

g = the fraction of C_0 applied to compartment 1 (-)
k_1 = rate constant for compartment 1 (d^{-1})
k_2 = rate constant for compartment 2 (d^{-1})

If $C_0 \times g$ is set equal to a and $C_0(1-g)$ is set equal to c, then the equation can be solved with R kinetics software for a, c, k_1, and k_2 by minimizing the objective function (S_{DFOP}) as described in equation 9.

DT_{50} and DT_{90} values can be calculated using equations 2 and 3, with k_1 or k_2 in place of k.

Objective Function: SFO, IORE, and DFOP are solved by minimizing the objective function (S_{SFO}, S_{IORE}, or S_{DFOP}).

$$S_{SFO}, S_{IORE}, \text{or } S_{DFOP} = \sum (C_{model,t} - C_{d,t})^2 \quad \text{(eq. 9)}$$

where,

S_{SFO} , S_{IORE}, or S_{DFOP} = objective function of kinetics model fit ($\%^2$)
n = number of data points (-)
$C_{model,t}$ = modeled value at time corresponding to $C_{d,t}$ (%)
$C_{d,t}$ = experimental concentration at time t (%)

Critical Value to Determine Whether SFO is an Adequate Kinetics Model

If S_{SFO} is less than S_C, the SFO model is adequate to describe kinetics. If not, the faster of t_{IORE} or the DFOP DT_{50} for compartment 2 should be used.

$$S_c = S_{IORE}\left(1 + \frac{p}{n-p} F(\alpha, p, n-p)\right) \quad \text{(eq. 10)}$$

where,

S_c = the critical value that defines the confidence contours ($\%^2$)
p = number of parameters (3 in this case)
α = the confidence level (0.50 in this case)
F(α, p, n-p) = F distribution with α level of confidence and degrees of freedom p and n-p